```
ATGAGCTATTACGGAAGTAGCTACCGGATTGTCAATGTGGACTCCAAATATCCAGGCTATCCTCC
AGAGCATGCCATCGCTGAGAAGAGAAGAGCAAGAAGGCGCTTGCTCCACAAAGATGGCAGCTGTA
ATGTGTACTTTAAACACATTTTTGGAGAATGGGGGAGCTACATGGTTGATATTTTTACCACTCTT
GTGGATACCAAGTGGCGCCATATGTTCATAATATTTTCTCTGTCTTACATTCTCTCCTGGTTGAT
ATTTGGTTCCATATTTTGGCTCATAGCCTTTCATCACGGAGACCTATTAAGCGATCCAGATATCA
CCCCTTGTGTTGACAACGTGCATTCATTTACGGCTGCATTTTTATTCTCCCTGGAGACCCAGACC
ACCATTGGATACGGTTACCGCTGTGTCACCGAAGAGTGCTCTGTGGCTGTACTGACAGTGATCCT
TCAGTCCATCCTCAGCTGCATCATAAACACCTTCATCATTGGAGCAGCCTTGGCAAAGATGGCAA
CTGCCCGGAAGAGAGCCCAGACCATACGCTTCAGCTATTTTGCCCTCATTGGTATGAGAGACGGG
AAGCCTTGCCTCATGTGGCGCATAGGTGACTTCCGACCAAACCATGTGGTAGAGGGCACGGTGAG
AGCCCAACTTCTGCGCTATTCAGAAGACAGTGAAGGGAGGATGACGATGGCGTTTAAAGACCTCA
AACTCGTCAATGACCAGATAATCCTGGTAACTCCAGTGACTATTGTCCATGAAATTGACCATGAG
AGCCCTCTGTATGCCCTTGACCGCAAGGCAGTGGCCAAAGATAATTTCGAGATTCTGGTGACATT
TATTTATACTGGTGATTCCACTGGGACATCCCACCAGTCCAGAAGTTCCTACATCCCCAGAGAAA
TTCTCTGGGGCCACAGGTTTCATGATGTATTGGAAGTGAAGAGAAAGTACTACAAGGTGAACTGC
TTGCAGTTTGAAGGAAGCGTGGAAGTCTACGCCCCCTTTTGCAGTGCCAAACAACTGGACTGGAA
GGACCAACAACTCAACAACTTGGAGAAAACGTCCCCTGCCCGAGGATCCTGCAATTCTGACACCA
ACACCAGGAGGCGGTCCTTCAGCGCAGTTGCCGTGGTGAGCAGCTGTGAGAACCCAGAGGAGACC
GTCCTGTCCCCACAAGATGAATGTAAGGAGATGCCCTATCAGAAAGCCCTCCTGACTTTAAATAG
GATCTCCATGGAATCCCAGATG (SEQ ID NO:1)
```

FIGURE 1

MSYYGSSYRIVNVDSKYPGYPPEHAIAEKRRARRRLLHKDGSCNVYFKHIFGEWGSYMVDIFTT
LVDTKWRHMFIIFSLSYILSWLIFGSIFWLIAFHHGDLLSDPDITPCVDNVHSFTAAFLFSLET
QTTIGYGYRCVTEECSVAVLTVILQSILSCIINTFIIGAALAKMATARKRAQTIRFSYFALIGM
RDGKPCLMWRIGDFRPNHVVEGTVRAQLLRYSEDSEGRMTMAFKDLKLVNDQIILVTPVTIVHE
IDHESPLYALDRKAVAKDNFEILVTFIYTGDSTGTSHQSRSSYIPREILWGHRFHDVLEVKRKY
YKVNCLQFEGSVEVYAPFCSAKQLDWKDQQLNNLEKTSPARGSCNSDTNTRRRSFSAVAVVSSC
ENPEETVLSPQDECKEMPYQKALLTLNRISMESQM (SEQ ID NO:2)

FIGURE 2

<u>underlined</u> = deleted in targeting construct

BOLD = sequence flanking Neo insert in targeting construct

ATGAGCTATTACGGAAGTAGCTACCGGATTGTCAATGTGGACTCCAAATATCCAGGCTAT
CCTCCAGAGCATGCCATCGCTGAGAAGAGAAGAGCAAGAAGGCGCTTGCTCCACAAAGAT
GGCAGCTGTAATGTGTACTTTAAACACATTTTTGGAGAATGGGGGAGCTACATGGTTGAT
ATTTTTACCACTCTTGTGGATACCAAGTGGCGCCATAT<u>GTTCATAATATTTTCTCTGTCT</u>
<u>TACATTCTCTCCTGGTTGATATTTGGTTCCATATTTTGGCTCATAGCCTTTCATCACGGA</u>
<u>GACCTATTAAGCGATCCAGATATCACCCCTTGTGTTGACAACGTGCATTCATTTACGGCT</u>
<u>GCATTTTTATTCTCCCTGGAGACCCAGACCACCATTGGATACGGTTACCGCTGTGTCAC</u>**C**
GAAGAGTGCTCTGTGGCTGTACTGACAGTGATCCTTCAGTCCATCCTCAGCTGCATCATA
AACACCTTCATCATTGGAGCAGCCTTGGCAAAGATGGCAACTGCCCGGAAGAGAGCCCAG
ACCATACGCTTCAGCTATTTTGCCCTCATTGGTATGAGAGACGGGAAGCCTTGCCTCATG
TGGCGCATAGGTGACTTCCGACCAAACCATGTGGTAGAGGGCACGGTGAGAGCCCAACTT
CTGCGCTATTCAGAAGACAGTGAAGGGAGGATGACGATGGCGTTTAAAGACCTCAAACTC
GTCAATGACCAGATAATCCTGGTAACTCCAGTGACTATTGTCCATGAAATTGACCATGAG
AGCCCTCTGTATGCCCTTGACCGCAAGGCAGTGGCCAAAGATAATTTCGAGATTCTGGTG
ACATTTATTTATACTGGTGATTCCACTGGGACATCCCACCAGTCCAGAAGTTCCTACATC
CCCAGAGAAATTCTCTGGGGCCACAGGTTTCATGATGTATTGGAAGTGAAGAGAAAGTAC
TACAAGGTGAACTGCTTGCAGTTTGAAGGAAGCGTGGAAGTCTACGCCCCCTTTTGCAGT
GCCAAACAACTGGACTGGAAGGACCAACAACTCAACAACTTGGAGAAAACGTCCCCTGCC
CGAGGATCCTGCAATTCTGACACCAACACCAGGAGGCGGTCCTTCAGCGCAGTTGCCGTG
GTGAGCAGCTGTGAGAACCCAGAGGAGACCGTCCTGTCCCCACAAGATGAATGTAAGGAG
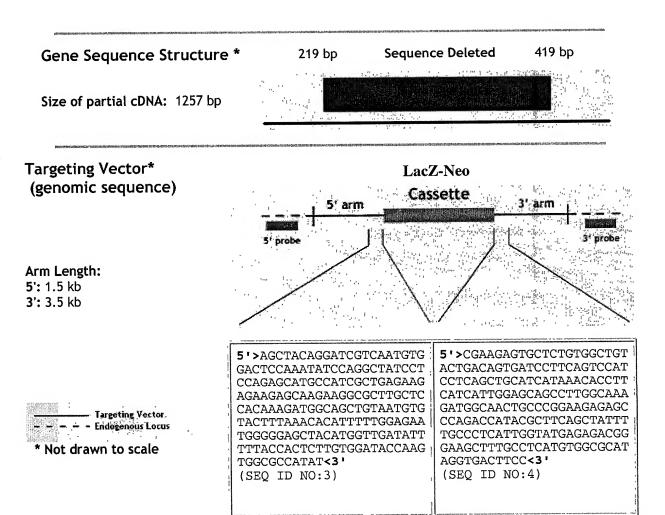ATGCCCTATCAGAAAGCCCTCCTGACTTTAAATAGGATCTCCATGGAATCCCAGATG

FIGURE 3

Gene Sequence Structure *

219 bp   Sequence Deleted   419 bp

Size of partial cDNA: 1257 bp

Targeting Vector*
(genomic sequence)

LacZ-Neo Cassette

5' arm   3' arm

5' probe   3' probe

Arm Length:
5': 1.5 kb
3': 3.5 kb

——— Targeting Vector
— — — — Endogenous Locus

* Not drawn to scale

5'>AGCTACAGGATCGTCAATGTG
GACTCCAAATATCCAGGCTATCCT
CCAGAGCATGCCATCGCTGAGAAG
AGAAGAGCAAGAAGGCGCTTGCTC
CACAAAGATGGCAGCTGTAATGTG
TACTTTAAACACATTTTTGGAGAA
TGGGGGAGCTACATGGTTGATATT
TTTACCACTCTTGTGGATACCAAG
TGGCGCCATAT<3'
(SEQ ID NO:3)

5'>CGAAGAGTGCTCTGTGGCTGT
ACTGACAGTGATCCTTCAGTCCAT
CCTCAGCTGCATCATAAACACCTT
CATCATTGGAGCAGCCTTGGCAAA
GATGGCAACTGCCCGGAAGAGAGC
CCAGACCATACGCTTCAGCTATTT
TGCCCTCATTGGTATGAGAGACGG
GAAGCTTTGCCTCATGTGGCGCAT
AGGTGACTTCC<3'
(SEQ ID NO:4)

FIGURE 4

Genotype	Age (Days)	Average Highest Voltage (volts)											
		No Stimulation	P080	P085	P090	P100	P110	P120	PP080P120	PP085P120	PP090P120	PP100P120	PP090P110
-/-	76	30.8	20.6	0.0	343.7	1198.3	1821.2	2315.9	1927.8	0.0	544.4	218.6	0.0
-/-	77	16.8	19.8	0.0	42.4	403.3	1154.4	1883.7	1476.6	0.0	1282.2	702.1	0.0
-/-	77	19.7	22.6	0.0	55.0	458.9	1751.5	2493.1	2036.3	0.0	716.4	207.1	0.0
-/-	78	35.8	50.3	0.0	79.1	381.4	1495.0	2250.3	1534.7	0.0	463.8	181.6	0.0
-/-	77	30.3	45.4	0.0	54.1	140.6	446.7	969.3	813.4	0.0	482.4	188.5	0.0
-/-	77	20.6	23.8	0.0	98.1	450.7	1840.5	2369.6	2639.2	0.0	1268.4	348.3	0.0
-/-	77	37.5	27.8	0.0	97.6	439.5	1367.7	1674.3	1670.8	0.0	437.6	122.0	0.0
-/-	73	42.4	34.2	0.0	112.3	378.5	1088.9	1800.2	1794.9	0.0	902.8	175.8	0.0
-/-	73	23.7	35.2	0.0	163.1	671.4	1753.9	1807.1	1256.9	0.0	823.3	272.6	0.0
+/+	78	51.1	62.5	0.0	38.9	115.2	976.7	1469.2	1429.2	0.0	701.6	168.0	0.0
+/+	76	16.4	19.7	0.0	25.1	486.3	1173.8	1577.7	1745.7	0.0	929.2	282.7	0.0
+/+	77	23.2	21.3	0.0	24.1	284.6	2023.0	2686.0	2379.4	0.0	1543.1	832.1	0.0
+/+	78	21.7	27.0	0.0	70.2	334.5	618.6	641.1	473.4	0.0	180.7	97.3	0.0
+/+	77	31.2	40.5	0.0	37.0	106.0	229.5	308.5	393.1	0.0	114.2	76.2	0.0
+/+	77	25.6	16.5	0.0	19.7	45.8	348.6	466.8	350.7	0.0	104.5	42.9	0.0
+/+	77	24.6	23.7	0.0	31.7	497.5	1420.5	1992.7	1677.8	0.0	1194.8	279.7	0.0
+/+	77	48.7	49.8	0.0	34.6	78.6	538.5	1738.3	1712.9	0.0	930.1	325.2	0.0
+/+	73	70.8	142.9	0.0	60.6	118.2	370.6	291.0	295.4	0.0	151.0	66.8	0.0
+/+	73	42.4	28.2	0.0	38.0	70.7	614.4	1312.0	861.8	0.0	791.3	180.7	0.0

FIGURE 5